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Case Report

Polyostotic Fibrous Dysplasia and Acromegaly

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Summary: A review of the recent orthopaedic literature reveals little information on the endocrinopathic associations of polyostotic fibrous dysplasia. This article illustrates the need for endocrinologic evaluations at both initial diagnosis and at follow-up examinations. Two patients with polyostotic fibrous dysplasia and acromegaly are presented. In both cases, diagnosis was made by endocrinologic and radiographic evaluations, including computed tomography (CT) scan of the skull. One patient had pituitary macroadenoma, and the other had pituitary microadenoma. Irradiation therapy was performed successfully in both patients without any complications. **Key Words:** Acromegaly—Fibrous dysplasia—McCune-Albright syndrome.

Polyostotic fibrous dysplasia, a rare condition of unknown etiology, is characterized by replacement of multiple bones by fibrous tissue. Two major variants of fibrous dysplasia exist: monostotic fibrous dysplasia and polyostotic fibrous dysplasia (9). Fibrous dysplasia primarily affects long bones and the skull, and it is one of the few nonmetabolic diseases that may involve the entire length of a long bone, from epiphysis to epiphysis. This condition is usually noted in childhood and frequently is arrested in adulthood (8). Unilaterality is a distinguishing feature but not a requisite for diagnosis. On radiographs, the involved bones typically have a ground glass appearance due to rarefaction, and proximal femoral involvement may result in coxa vara and shepherd's crook deformity. In addition, tibial bowing and protrusio acetabulae may occur, and pathologic fractures are frequent. Changes in the cranium may be confusing. The base of the skull may show hyperostotic growth, obliterating the sella turcica and resulting in the characteristic signs and symptoms of a slow-growing intracranial space-occupying lesion (2).

In 1937, McCune and Bruch and Albright et al. separately described polyostotic fibrous dysplasia associated with café-au-lait pigmentation, typical bone lesions, and precocious puberty in females (1,15). Since then, multiple reports on endocrinopathies have described this syndrome, its unexplained pathogenesis, and the relationship between skeletal and endocrine abnormality (sexual precocity, hyperparathyroidism, hyperthyroidism, acromegaly, and Cushing's disease) (6,7,11,13,14, 17,18). However, few reports have described the orthopaedic implications of this disorder. We describe the endocrinopathic and orthopaedic implications of polyostotic fibrous dysplasia and acromegaly in two patients with McCune-Albright syndrome.

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CASE REPORTS

Case 1

A 27-year-old white man had been diagnosed with polyostotic fibrous dysplasia after investigation of a limp when he was 7 years old. He had a normal childhood and no family history of fibrous dysplasia. Initial diagnosis was made by radiographic examination and bone biopsy. Since then, he has had one fracture of the right femur, two supracondylar fractures of the left humerus, and multiple fractures of the left proximal femur. He underwent four valgus osteotomies of the left femur with bone grafting to correct a shepherd's crook deformity (Fig. 1). In addition, problems with his right knee associated with loose bodies resolved after operative excision. His back appeared straight. The patient developed a limb length discrepancy ~4 cm. The right limb was longer and showed varus deformity. This was compensated by an equinus left foot. He has not been free of ambulatory aids since age 13 years and has recently begun walking with one crutch.

The patient was generally taller than his peers and grew into the 95th percentile for height. Onset of puberty occurred at age 11 years. He has worn a size 13 shoe for the past 10 years. The patient de-

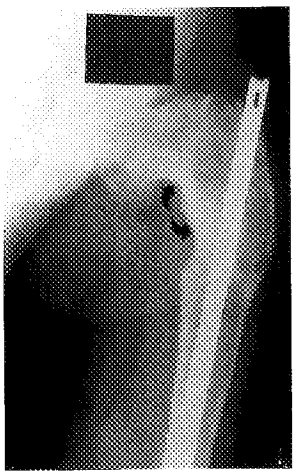

FIG. 1. Anteroposterior radiograph of shepherd's crook and coxa vara deformity.

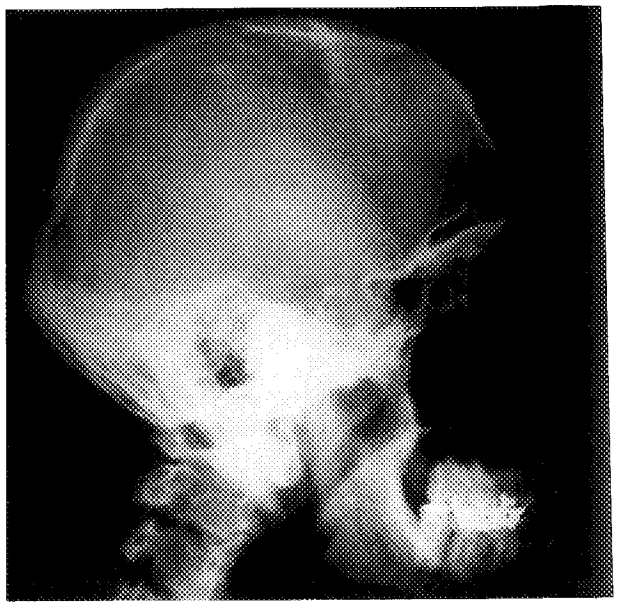

FIG. 2. Lateral radiograph of the skull showing eroded floor of sella turcica.

nied any recent or remote changes in his libido, which he has not considered significantly different from that of his peers throughout his life. He denied any symptoms of visual field changes, headaches, or impaired hearing. His mother was 160 cm tall, his father was 168 cm tall, and his two brothers aged 24 and 23 years were 173 and 183 cm tall, respectively. At age 27 years, the patient was 191 cm tall and weighed 185 lbs.

At last follow-up physical examination showed coarse facial features, wide spacing of the teeth in his lower jaw, an underbite, and large hands with truncated fingers. His blood pressure was 130/90, and his pulse rate was 80 beats/min. Chest and abdominal examinations were normal. His thyroid gland was not enlarged, and no papilledema was noted in his eye grounds. Visual fields were normal. Genitalia were Tanner 5; his right and left testes both measured 4.5 cm.

Radiographic examination showed extensive involvement of the left proximal femur with a femoral neck fracture. A ground-glass density was apparent with a relative increase in the diameter of the medullary space. Radiographs of the hands showed chronic changes in the fingers and distal radius consistent with fibrous dysplasia. Films of the skull showed overgrowth of the paranasal sinus and an enlarged mandible. Computed tomography (CT) scan of the sella turcica revealed a contrast-enhancing intrasellar mass eroding the floor of the sella turcica, consistent with an enlarging pituitary tumor (Fig. 2).

Endocrine evaluation of serum T3, T4, FTI, luteinizing hormone, testosterone, PTH-D and PTH-N terminal, along with 24-h collections of urinary calcium, cortisol, creatinine, phosphorus, and 25-hydroxy vitamin D were all within normal limits. Alkaline phosphatase was 568 IU/dl (normal 50–136 IU/dl), and prolactin was 38.6 ng/dl. The electrolyte, serum calcium, and serum phosphate levels were normal. Fasting growth hormone level was elevated at 23 ng/ml (normal <10 ng/ml). Furthermore, growth hormone was not suppressed during glucose tolerance testing, as in normal persons.

The final diagnosis was polyostotic fibrous dysplasia with acromegaly due to a pituitary adenoma that was secreting excess growth hormone and prolactin. Pituitary irradiation was performed successfully without any toxic side effects (12). The patient was followed, with no detectable changes in his facial features or hands. At last follow-up, he had persistent left hip pain, was dependent on a crutch for ambulation, and was receiving testosterone supplementation.

Case 2

A 21-year-old Hispanic man had been examined by an orthopaedic surgeon at the age of 7 years because of right hip and knee pain. Radiographs at that time showed a lesion on the right femur, which was treated by curettage and bone graft. Bone biopsy confirmed the diagnosis of fibrous dysplasia. Subsequently, the patient developed pain and degenerative joint disease of the right ankle (Fig. 3). Fusion was performed because of severe disability and failure of conservative treatment. Degenerative changes at the right hip (Fig. 4) and knee were also noted.

The patient had a normal birth and childhood. Puberty began at age 15 years. He denied any headache, vomiting, polydipsia, or history of visual complaints. At the time of presentation, he was not taking any medication. Physical examination showed an extremely tall (198 cm) and obese (375 pounds) patient with the typical coarse features of acromegaly (Fig. 5A and B). No other family mem-

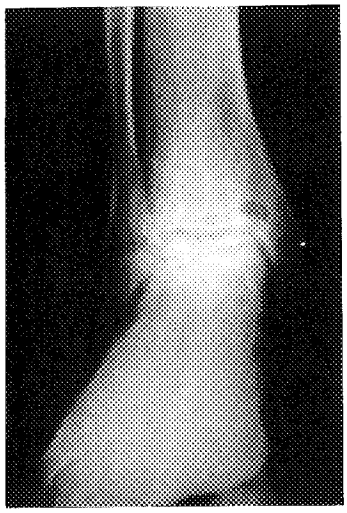

FIG. 3. Anteroposterior radiograph showing degenerative changes of the right ankle. The patient subsequently underwent arthrodesis.

ber was taller than 152 cm. His blood pressure was 130/80, and his heart rate was 88 beats/min. Neurologic examination was normal, as were cardiac, abdominal, and pulmonary examinations. The patient walked with a limp on the right and had a fixed external rotation deformity of the right lower extremity. Shoulders, elbows, and wrists showed full range of motion. Café-au-lait spots on his back displayed the typical "coast of Maine" appearance.

When the patient was 18 years old, he had been referred for endocrinologic evaluation. Ophthalmologic examination of his visual fields showed a defect consistent with a chiasmal lesion. Laboratory results showed complete blood count, urine examination, total protein, albumin, and fasting glucose levels all to be within normal limits. Urine specific gravity after 12-h of fluid restriction was 1.028. Alkaline phosphatase was elevated to 204 IU/dl. Electrolytes were within normal limits. A complete endocrine evaluation was performed, including serum levels of growth hormone, fasting growth hormone, somatotropin, prolactin, testosterone, adrenocorticotropic hormone, cortisol, follicle-stimulating hormone, luteinizing hormone, and complete thyroid function (T3, T4, and TSH), along with 24-h urine collections for cortisol and calcium. The following were abnormal: fasting growth hormone was elevated to 10.0 ng/ml (normal <10 ng/ml) and glucose levels remained unsuppressed after oral glucose tolerance testing; somatotropin was elevated to 3.8 μg/ml (normal 0.34–1.9 μg/ml); and testosterone levels were low at 117.0 μg/dl (normal ≥280 μg/dl). Serum calcium was 9.7 mg/dl, and phosphate was 5.23 mg/dl.

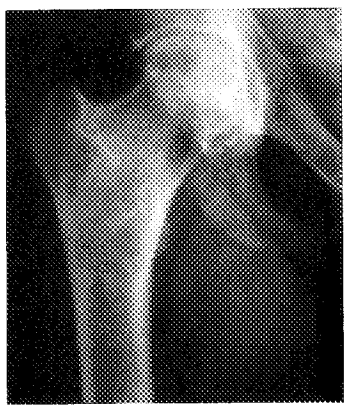

FIG. 4. Anteroposterior radiograph of pelvis showing characteristics of fibrous dysplasia involving right proximal femur and pelvis with degenerative changes of right hip joint.

Radiographic findings of the upper extremities were normal except for a small area of lysis and sclerosis along the medial aspect of the proximal right humerus. However, the right lower extremity showed fibrous dysplasia involving multiple bones. Radiographs of the skull showed an enlarged paranasal sinus region, a large mandible, widely spaced teeth, a thickening of the calvarium, but a normal sella turcica (Fig. 6). Polytomography and CT examination showed no apparent mass.

The final diagnosis was polyostotic fibrous dysplasia secondary to pituitary microadenoma. Irradiation was performed successfully without complication (12). The patient was followed with no medication and at last follow-up had a persistent limp and ambulated with a crutch.

DISCUSSION

The classic McCune-Albright syndrome has been characterized by predominantly unilateral polyostotic fibrous dysplasia, café-au-lait spot pigmentation, and sexual precocity in females. In the few reports of McCune-Albright syndrome in males, sexual precocity has seldom been observed (4,6, 13,17,18). There may be many other endocrine abnormalities associated with McCune-Albright syndrome less frequently reported and therefore not widely appreciated, especially in the orthopaedic literature. These abnormalities may include hyperthyroidism, hyperparathyroidism, Cushing's disease, diabetes mellitus, and acromegaly, in addition to sexual precocity. The two patients described in this report had acromegaly associated with polyostotic fibrous dysplasia.

The diagnosis of acromegaly associated with polyostotic fibrous dysplasia can be difficult (2,16). Acromegalic patients may have a history of progressive increases in shoe and hat sizes after puberty, as did Case 1. If excessive secretion of growth hormone occurs before skeletal maturity, pituitary giantism occurs and the patient is usually above the 95th percentile for height and weight. Because of the slow progressive nature of acromegaly, clinical features such as large nose, thick lips, prominence of forehead and orbital ridge, wide spacing of teeth, large mandible with underbite,

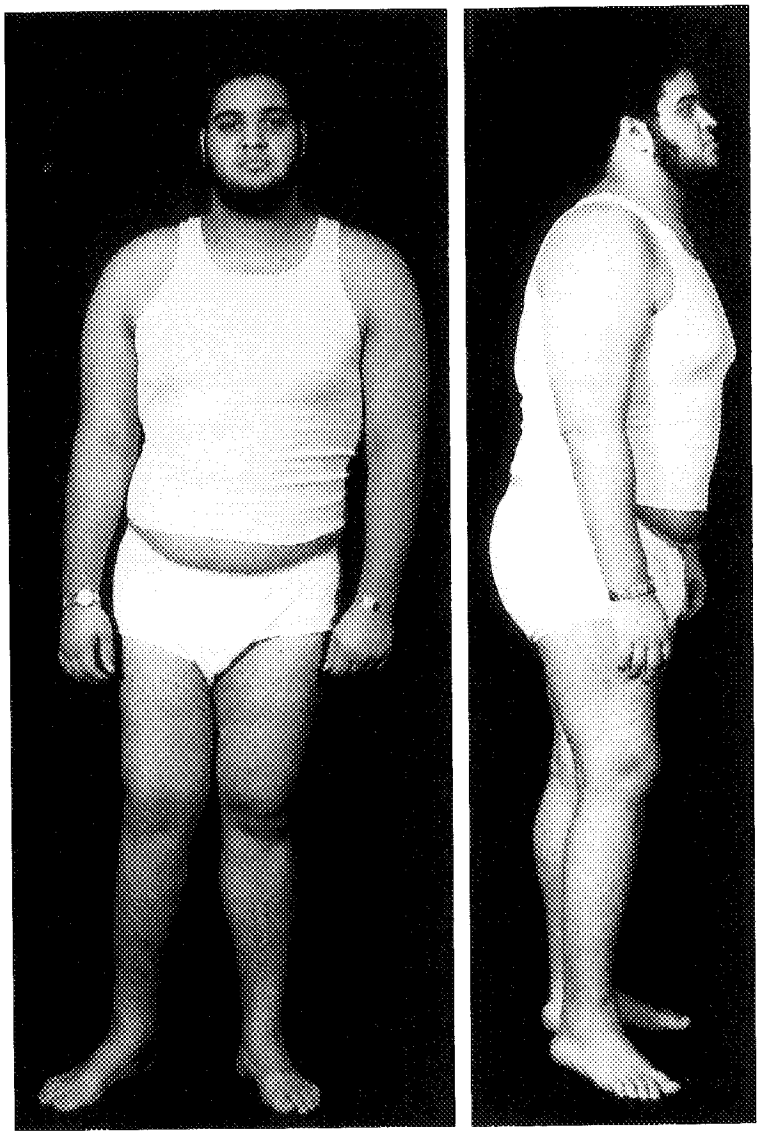

FIG. 5. Front **(A)** and side view **(B)** photographs showing coarse features of acromegaly.

broad hands and feet, and coarse skin and hair may not be noticed by the patient.

Symptoms of myopathy and peripheral neuropathy, such as weakness and paresthesia, may be associated with acromegaly. Osteoarthrosis may occur early and be aggravated by the process of fibrous dysplasia as well. Hypertension, glucosuria, polydipsia, and polyphasia occur in ~25% of patients (11). Visual field abnormality caused by pituitary adenoma or by skull involvement of fibrous dysplasia is common, and ophthalmologic examination is recommended (2). Radiographic findings often show enlargement of the paranasal sinus, thickening of the base of the skull, enlargement of the mandible, and enlargement or ballooning of the sella turcica. Endocrinologic investigations are essential to rule out other abnormal conditions, such as Cushing's disease, diabetes, hyperthyroidism, and hyperparathyroidism. Serum calcium phosphate is usually normal in acromegalic patients;

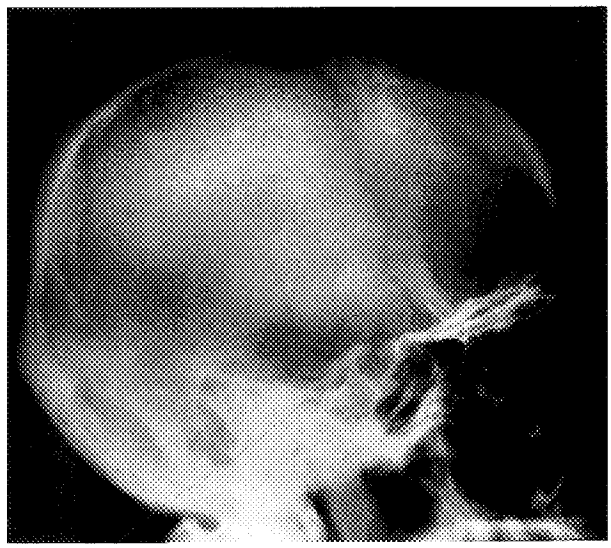

FIG. 6. Lateral radiograph of skull showing normal sella turcica but thickening of the calvarium.

however, phosphate may be elevated from excess growth hormones (11).

Peripheral joint manifestations of acromegaly are well described (3,5,10). Knees, hips, and shoulders appear to be most commonly affected by acromegalic arthropathy, and late joint deformity may require joint arthroplasty. This particular type of arthropathy may be associated with joint enlargement, synovium thickening, and bony overgrowth and deformity with loss of motion. The histologic picture is one of articular cartilage hypertrophy and hyperplasia leading to disruption of joint geometry (10). Treatment is directed at identifying and eradicating the cause of excess growth hormone production.

Skeletal manifestations of fibrous dysplasia are perhaps more easily recognized. Varus deformity of the femoral neck and shepherd's crook deformity of the proximal femur are common. Bowing or pathologic fractures of long bones and osteoarthrosis of multiple joints must be addressed individually, as in our two patients. The mainstay of operative intervention includes osteotomies with bone grafting and internal fixation. Limb length discrepancy in some cases may necessitate limb lengthening or epiphyseodesis, depending on the magnitude of the discrepancy.

Characteristic symptoms of bone involvement in acromegaly may mimic those of polyostotic fibrous dysplasia, making concurrent diagnosis difficult unless specifically sought. Because of late diagnosis, both patients had severe destructive changes of multiple joints. Extreme obesity, long bone deformity in proximity to weightbearing arthritic joints, and limb length discrepancy at a young age are now particular problems that ultimately must be addressed by the reconstructive surgeon in both these patients.

CONCLUSION

McCune-Albright syndrome consists of the triad of polyostotic fibrous dysplasia, café-au-lait pigmentation, and a wide variety of endocrinopathies. The clinical picture, diagnostic investigation, and management of two patients with polyostotic fibrous dysplasia and acromegaly are described. In addition to appropriate orthopaedic management of impending fracture, deformity, and pain, the possibility of an associated endocrinologic abnormality specifically must be addressed. If untreated (acromegaly), the incidence of cardiovascular complications such as cardiomegaly, congestive heart failure, hypertension, and renal failure is increased. These patients are also prone to psychological disturbances and almost always have emotional lability. Diabetes mellitus, visual field defect, and auditory dysfunction may also occur. The orthopaedist must be aware of these endocrine associations so that proper referral and treatment may be instituted. Finally, polyostotic fibrous dysplasia does not decrease life expectancy, but acromegaly may.

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